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13. ABSTRACT *(Maximum 200 words)*

We sought to determine if 1) peak vascular conductance (Gmax) of the calf was reduced following exposure to prolonged simulated microgravity and 2) if maximal cycle ergometry performed at the end of microgravity exposure stimulated a restoration of Gmax. To do this, Gmax was recorded following ischemic plantar flexion exercise to fatigue in seven men after 16 days of head-down tilt (HDT) under two conditions: 1) after one bout of maximal supine cycle ergometry completed 24 h prior to performance of ischemic plantar flexion exercise, and 2) in a control (no cycle ergometry) condition. Following HDT, Gmax was reduced in the control condition (0.38 ± 0.02 to 0.24 ± 0.02 ml/100 ml/min/mmHg; $P = 0.04$), but was restored when subjects performed cycle ergometry (0.33 ± 0.05 to 0.28 ± 0.04 ml/100 ml/min/mmHg). After HDT time to fatigue during ischemic plantar flexion exercise was not different from pre-HDT 24 h after performance of exhaustive cycle ergometry (120 ± 24 vs. 122 ± 19 sec), but was decreased in the control condition (116 ± 11 vs. 95 ± 8 sec; $P = 0.07$). These data suggest that a single bout of maximal exercise can provide a stimulus to restore Gmax and maintain time to fatigue during performance of ischemic plantar flexion exercise.

14. SUBJECT TERMS

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Restoration of peak vascular conductance after simulated microgravity by maximal exercise

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Summary

We sought to determine if (i) peak vascular conductance of the calf was reduced following prolonged exposure to simulated microgravity, and (ii) if maximal cycle ergometry performed at the end of microgravity exposure stimulated a restoration of peak calf vascular conductance. To do this, peak vascular conductance of the calf was recorded following ischaemic plantar flexion exercise to fatigue in seven men after 16 days of head-down tilt (HDT) under two conditions: (i) after one bout of maximal supine cycle ergometry completed 24 h prior to performance of ischaemic plantar flexion exercise, and (ii) in a control (no cycle ergometry) condition. Following HDT, peak vascular conductance was reduced in the control condition ($0{\cdot}38 \pm 0{\cdot}02$ to $0{\cdot}24 \pm 0{\cdot}02$ ml 100 ml^{-1} min^{-1} mmHg^{-1}; $P = 0{\cdot}04$), but was restored when subjects performed cycle ergometry ($0{\cdot}33 \pm 0{\cdot}05$ to $0{\cdot}28 \pm 0{\cdot}04$ ml 100 ml^{-1} min^{-1} mmHg^{-1}; $P = 0{\cdot}46$). After HDT, time to fatigue during ischaemic plantar flexion exercise was not different from pre-HDT 24 h after performance of exhaustive cycle ergometry (120 ± 24 vs. 122 ± 19 s), but was decreased in the control condition (116 ± 11 vs. 95 ± 8 s; $P = 0{\cdot}07$). These data suggest that a single bout of maximal exercise can provide a stimulus to restore peak vascular conductance and maintain time to fatigue during performance of ischaemic plantar flexion exercise.

Keywords: bedrest, blood flow, fatigue, hyperaemia, vasodilation.

Introduction

Exposure to low gravity or bedrest leads to marked reductions in functional work capacity (Saltin *et al.*, 1968; Convertino *et al.*, 1982a, 1982b; Blomqvist & Stone, 1983; Convertino, 1987), which may seriously reduce exercise capacity in patients after prolonged inactivity as well as impact the ability of space crews to perform egress manoeuvres in the event of an emergency. Previous investigations have revealed that microgravity-induced decrements of aerobic power can be partially attributed to impaired central cardiovascular function consequent to depletion of plasma volume (Saltin *et al.*, 1968; Convertino *et al.*, 1982a, 1982b; Blomqvist & Stone, 1983) and decreased oxidative enzyme activity in peripherally active tissue (Hikida *et al.*, 1989). A single bout of supine cycle exercise to exhaustion performed immediately prior to re-ambulation from 10 days of simulated microgravity returned aerobic power to pre-bedrest levels within 3 h (Convertino, 1987). Although the underlying mechanism of this response

was not identified, it was proposed that acute sensitization of cardiovascular reflexes and repletion of plasma volume may be responsible for restoration of aerobic capacity (Convertino, 1987). Alternatively, it is possible that fatiguing cycle ergometry altered vascular dynamics of the legs, thus enhancing blood flow to active muscle. Although baseline resting blood flow is reduced by exposure to simulated microgravity (Blamick *et al.*, 1988; Convertino *et al.*, 1989, 1994), we are unaware of any investigations in which change in maximal vasodilatory capacity and its relationship with aerobic power have been reported following exposure to a low-gravity analogue. Understanding the impact of low gravity on maximal vasodilatory capacity in working muscles is relevant since maximum oxygen uptake is influenced by vascular conductance (Snell *et al.*, 1987; Martin *et al.*, 1991; Reading *et al.*, 1993; Kosmas *et al.*, 1996). Therefore, we tested the hypotheses that (i) exposure to a ground-based simulation of low gravity elicits a reduction in peak vascular conductance, and (ii) this effect can be ameliorated by performance of a single bout of cycle ergometry.

Subjects and methods

Subjects

Seven asymptomatic, non-smoking, normotensive men with physical characteristics similar to the astronaut corps (means ± 1 standard error of the mean (± SE) age 40 ± 2 years, height 183 ± 2 cm, weight 81 ± 2 kg, peak oxygen uptake 2·9 ± 0·4 l min^{-1}) gave their written consent to serve as subjects for this investigation after they had been informed of all procedures and risks. All procedures were approved by the Human Research Review Boards of the National Aeronautics and Space Administration (NASA) at Kennedy Space Center, NASA-Ames Research Center, and Brooks Air Force Base. Selection of subjects was based on results of a screening evaluation comprised of a detailed medical history, physical examination, blood chemistry analysis, urinalysis, chest X-ray, and resting and treadmill electrocardiogram. During an orientation session conducted prior to the study, all subjects were made familiar with the laboratory personnel, procedures and protocols.

Experimental design

A randomized, cross-over design was used in which subjects completed two 16-day head-down tilt (HDT) periods separated by 11 months (July 1992 and June 1993). During the first experimental period, four subjects performed a single bout of exercise on day 16 of HDT (treatment condition) while three subjects did not exercise during HDT (control condition). During the second experimental period, the three subjects who underwent the control condition in the first experimental period performed a single bout of exercise on day 16 of HDT while four subjects who exercised in the first experimental period underwent the control condition.

Experimental protocol

The experimental protocol consisted of 4 days of ambulatory control followed by 16 days of 6° HDT and 2 days of post-HDT recovery (Fig. 1). The 16-day HDT period was chosen because it represents maximum duration for current space shuttle missions. The 6° HDT posture was chosen because changes in numerous cardiovascular functions elicited by this posture are similar to those seen in actual spaceflight (Convertino, 1995). During both HDT periods, subjects lived 24 h per day in the Human Research Facility at NASA-Ames Research Center, remained head-down without interruption for all daily activities, and followed the same controlled diet. All

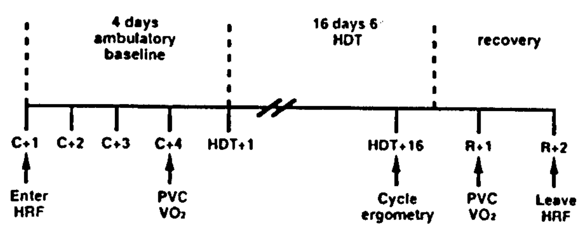

Figure 1 Experimental protocol time-line. Each subject (n = 7) completed two 16-day periods of 6° HDT separated by 11 months – one in the exercise condition and one in the control condition. HDT, head-down tilt days 1–16; C, pre-HDT baseline period; R, post-HDT recovery period; HRF, Human Research Facility at NASA-Ames Research Center; PVC, peak calf vascular conductance following ischaemic plantar flexion exercise; VO_2, peak oxygen uptake exercise test; cycle ergometry, maximal supine cycle ergometry performed in the EXERCISE condition.

measurements were conducted at the same time of day and in the same sequence before, during and after HDT. All subjects abstained from alcohol, caffeine, medication and conventional exercise for the duration of the study.

Leg blood flow and time to fatigue during ischaemic plantar flexion exercise were measured on the fourth pre-HDT control day (C + 4) and at the end of 16 days of HDT just prior to re-ambulation (day R + 1; Fig. 1). The ischaemic plantar flexion exercise testing was completed in ≈ 30 min. Each subject performed a single bout of graded supine cycle exercise designed to elicit maximal effort 24 h prior to the R + 1 measurements of leg blood flow and time to fatigue during one of the HDT exposures (exercise condition). Following the other, subjects did not exercise (control condition). Subjects underwent an orthostatic tolerance test to lower body negative pressure (Engelke *et al.*, 1996) just prior to ischaemic plantar flexion exercise testing during both the exercise and the control conditions.

Ischaemic calf exercise

Plantar flexion exercise was performed in the supine posture with the right leg placed in an adjustable brace which stabilized and isolated the lower limb (Fig. 2). The calf exercise task required that subjects press against a stationary footplate at a rate of 60 contractions min^{-1} and produce a target force of 588 N $contraction^{-1}$ (60 kg $contraction^{-1}$). Force production was measured by a transducer placed in series with the foot pedal. A monitor placed within view of the subject provided instantaneous feedback on force production. Cadence was maintained with the assistance of a metronome. During calf exercise, the lower limb was made ischaemic by inflation (to 300 mmHg) of a pneumatic cuff placed just above the knee. The exercise bout was terminated when subjects were unable to maintain the required cadence and/or force production for ≥5 s. At volitional fatigue, pressure in the thigh cuff was released and measurement of post-ischaemic blood flow commenced within 10 s.

Leg blood flow

Leg (calf) blood flow was measured by venous occlusion plethysmography using a calibrated mercury-in-silastic strain gauge placed around the maximum diameter of the right calf. Circulation to the foot was occluded with a cuff placed at the distal end of the lower leg and venous efflux was impeded by a second cuff placed on the thigh just above the knee. With blood flow to the foot occluded by inflation of the distal cuff to 300 mmHg, the thigh cuff was inflated to 60 mmHg for 10 s followed by 10 s of deflation. Blood flow was calculated as the average slope of the linear portion of the first three pulse beats on the plethysmographic tracing for each occlusion. Care was taken to exclude any artefacts resulting from the rapid

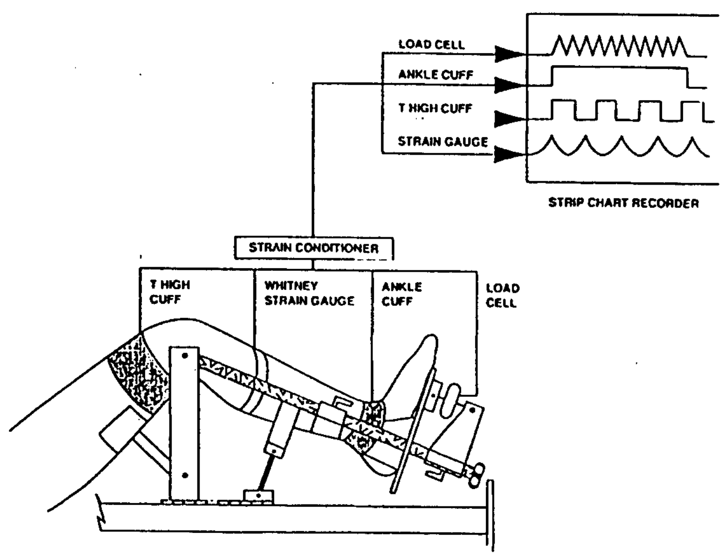

Figure 2 Schematic of brace used to stabilize the right leg during performance of ischaemic plantar flexion exercise.

inflation of the occlusion cuff. Resting leg blood flow was determined by averaging nine flow measurements recorded over 3 min immediately prior to initiation of ischaemic calf exercise. At the conclusion of plantar flexion exercise, 12 flow measurements over 4 min were made with the greatest response chosen as representative of the peak flow. All individual peak blood flows occurred by the fourth measurement (i.e. 70 s) for all subjects. These represented valid peak blood flows under all experimental conditions since average peak blood flows for all subjects under all experimental conditions did not decline until after 90 s (Fig. 3). Peak vascular conductance was calculated by dividing the peak post-ischaemia blood flow by the mean arterial pressure (systolic blood pressure plus twice diastolic divided by three) measured with an automated blood pressure device during the exercise.

Exercise bouts

When in the exercise condition, all subjects performed a multistage exercise bout to exhaustion on day HDT + 16 utilizing a Quinton supine cycle ergometer. After a 4-min warm-up at 32 W, exercise intensity was increased by 16 W^{-1} min until the subject reached volitional fatigue and was unable to maintain a pedalling cadence of 60–70 revolutions min^{-1} for a period exceeding 15 s. A tachometer placed at eye level assisted the subject in maintaining the required cadence. Heart rate was recorded during the last 15 s of each minute while blood pressure was measured by brachial artery auscultation before and immediately after exercise. Subjects were verbally encouraged to achieve a maximal effort. For the seven subjects, final workload at volitional fatigue averaged 241 ± 14 W and was attained after a mean time of 16·0 ± 0·8 min. Heart rate and systolic and diastolic blood pressures at termination averaged 182 ± 3 beats min^{-1}, 177 ± 6 mmHg and 77 ± 4 mmHg, respectively. Additionally, all subjects completed a similar exercise bout before and after HDT immediately following the ischaemic calf exercise to determine peak oxygen uptake. During these tests, oxygen uptake was determined by analysis of expired air using calibrated electronic analysers.

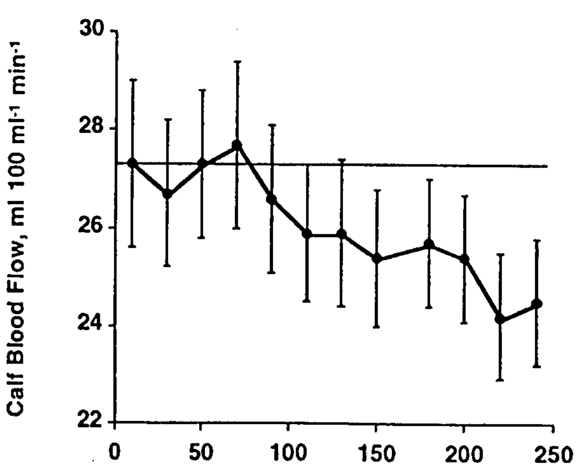

Figure 3 Time-course of peak blood flow in the calf during the 4 min following ischaemic plantar flexion exercise to fatigue. Each data point represents the mean (closed circles) ± 1 SE (bars) of all tests under all conditions.

Statistical analysis

Standard descriptive statistics were calculated on all response variables of interest and are expressed as means ± 1 standard error (± SE). The effects of HDT and maximal cycle ergometry on peak blood flow and vascular conductance after ischaemic calf exercise were evaluated using a two-way analysis of variance for repeated measures. Student–Newman–Keuls multiple comparisons technique was used to identify the location of differences between means. Least-squares linear regression was used to examine the relationship between peak oxygen uptake and peak vascular conductance.

Results

Leg blood flow and mean arterial pressure

Prior to HDT, there was no statistically significant difference in resting leg blood flow between exercise and control conditions. Following HDT, resting leg blood flow was reduced in both experimental conditions (from 2·4 ± 0·2 to 1·5 ± 0·2 and 2·2 ± 0·1 to 1·4 ± 0·2 ml 100 ml^{-1} min^{-1} for control and exercise, respectively; $P = 0.004$). Before HDT, no statistically significant difference was observed in peak calf blood flow induced by ischaemic exercise between experimental conditions. Following HDT, peak calf

blood flow was reduced by 25% in the control condition (33·4 ± 1·4 to 24·9 ± 2·3 ml 100 ml^{-1} min^{-1}; P = 0·04), but was unchanged following performance of cycle ergometry on HDT day 16 (29·2 ± 4·2 vs. 27·1 ± 3·7 ml 100 ml^{-1} min^{-1}; P = 0·72). Mean arterial blood pressure at the end of ischaemic calf exercise did not differ statistically (F = 1·872; P = 0·161) between pre-HDT control (89 ± 3 mmHg), post-HDT control (97 ± 8 mmHg), pre-HDT exercise (88 ± 2 mmHg) and post-HDT exercise (96 ± 3 mmHg) conditions.

Peak vascular conductance

Prior to HDT, there was no statistically significant difference in peak vascular conductance between conditions (Fig. 4A). Following HDT, peak vascular conductance was reduced in the control condition (P = 0·04), but was not statistically lowered following performance of cycle ergometry on HDT day 16 (P = 0·46; Fig. 4A). The reduction in peak vascular conductance during ischaemic plantar flexion exercise from pre-HDT to post-HDT was less in 5 of the 7 subjects with exercise treatment, and was increased following exercise in two subjects (Fig. 4B).

Fatigue index

Time to fatigue during ischaemic leg exercise was unchanged after HDT when exercise was performed (120 ± 24 vs. 122 ± 19 s), but was decreased (P = 0·07) in the control condition (116 ± 11 vs. 95 ± 8 s).

Peak oxygen uptake

Peak oxygen uptake decreased from 2·7 ± 0·2 at pre-HDT to 2·3 ± 0·1 l min^{-1} at day 16 of HDT

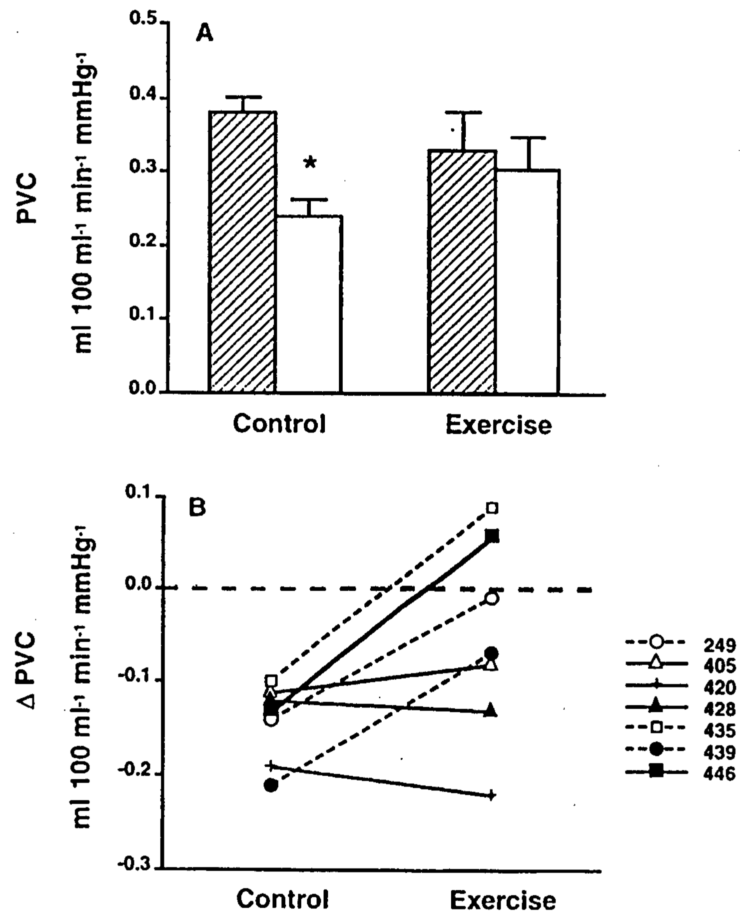

Figure 4 (A) Peak vascular conductance (PVC) elicited by ischaemic calf exercise before (hashed bars) and after (open bars) 16 days HDT in the exercise and control conditions. Bars represent ± 1 SE and asterisks indicate P < 0·05 vs. pre-HDT value. (B) Comparisons of the change in peak vascular conductance (ΔPVC) from pre-HDT (zero) for each of the seven subjects under the control and exercise conditions.

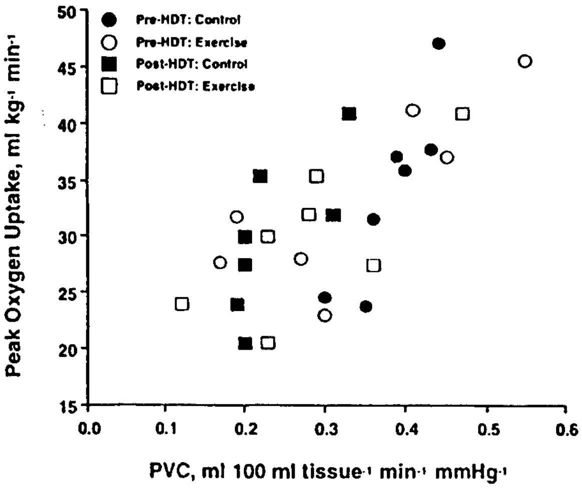

Figure 5 Relationship between peak vascular conductance (PVC) and peak oxygen uptake (r = 0·73, P = 0·001).

(P = 0·006) in both conditions. The peak oxygen uptake 24 h after maximal exercise increased slightly in 5 of 7 subjects (mean 2·4 ± 0·2 l min^{-1}), but was not statistically different from 2·3 ± 0·1 l min^{-1} (P = 0·826) in the control condition and remained lower (P = 0·0002) than pre-HDT. The correlation coefficient describing the relationship between peak vascular conductance and peak oxygen uptake was r = 0·73 across all conditions (P = 0·001; Fig. 5).

Discussion

In the present study, we observed that 16 days of continuous HDT reduced resting and peak leg blood flow and vascular conductance in the calf. Peak leg blood flow and vascular conductance were restored to pre-HDT levels when a single bout of exhaustive supine cycle ergometry was performed 24 h prior to completion of ischaemic calf exercise. Since we measured peak leg blood flow and vascular conductance only once after maximal exercise, we do not know the duration of the exercise effect. Therefore, our conclusions are limited to the 24-h period after cycle exercise. Our data also indicate that subjects with the highest peak vascular conductance exhibited the greatest peak aerobic power, confirming previous reports that lower leg vascular conductance is strongly associated with peak aerobic capacity (Snell *et al.*, 1987; Martin *et al.*, 1991; Reading *et al.*, 1993; Kosmas *et al.*, 1996).

Resting leg blood flow was reduced by 40% after 16 days of uninterrupted confinement to the 6° HDT posture. This observation is in accordance with similar reports of reduced resting blood flow in the calf (Blamick *et al.*, 1988; Convertino *et al.*, 1989, 1997) and forearm (Convertino *et al.*, 1994) following exposure to a ground simulation of microgravity. Despite its effects on peak vascular conductance, performance of exhaustive supine cycle ergometry had no effects on resting leg blood flow, suggesting that control of resting and peak leg blood flow are different. This may be due to the influence of vasodilator metabolites which are produced during ischaemic plantar flexion exercise but are not present in the resting state.

The mechanisms responsible for restoration of peak leg blood flow and vascular conductance to pre-HDT levels following performance of exhaustive supine cycle ergometry are not clear. However, our observation is consistent with data demonstrating that the rate of elevation in vascular conductance at the onset of exercise is increased with short-term exercise training (Shoemaker *et al.*, 1996). The restoration may be the result of plasma volume expansion elicited by the bout of maximal cycle exercise. Similar to previous reports of marked hypovolaemia following microgravity exposure (Convertino *et al.*, 1982a, 1982b, 1994; Blomqvist & Stone, 1983; Convertino, 1995), we observed a 16% reduction in plasma volume after 16 days of HDT in the subjects of the present study (Convertino *et al.*, 1996). However, plasma volume was completely restored to pre-HDT levels in our subjects within 24 h following completion of the maximal exercise bout (Convertino *et al.*, 1996). Since plasma volume expansion was associated with increased cardiac output in our subjects (Engelke *et al.*, 1996) it is possible that a greater quantity of blood was available for perfusion of active muscle in the exercise condition. Volume expansion may have also altered baroreflex control of vascular resistance. Consistent with this hypothesis is the observation of a strong inverse relationship between plasma volume and vascular resistance in humans (Thompson *et al.*, 1990; Mack *et al.*, 1991) and rabbits (Ludbrook & Graham, 1984). Therefore it is possible that exercise-induced expansion of plasma volume elicited a baroreflex-mediated reduction in systemic resistance leading to greater perfu-

sion of the leg vasculature following ischaemic calf exercise.

Another factor that may have contributed to the restoration of peak vascular conductance is vasodilator metabolites which are produced when a mismatch between blood flow and exercise intensity exists (Sparks, 1980). These substances mediate a substantial hyperaemia upon restoration of blood flow to previously ischaemic tissue (Sparks, 1980). The degree of hyperaemia is dependent on the duration of the ischaemia and intensity of activity performed during the period of ischaemia (Patterson & Whelan, 1955). In the present study, although the same functional endpoint was achieved (i.e. fatigue), the average duration of ischaemic plantar flexion exercise was 27 s longer following HDT in the exercise condition. This may suggest that the 22% longer period of circulatory arrest resulted in greater accumulation of vasodilatory metabolites, thus facilitating a greater hyperaemic response when circulation was restored. It is possible that restoration of peak vascular conductance may be explained by an exercise-induced increase in vascular sensitivity to vasodilator metabolites. However, it remains to be determined whether production and subsequent accumulation of metabolites during a bout of high-intensity ergometry can increase the vascular responsiveness to these agents following subsequent performance of ischaemic plantar flexion exercise.

There is compelling evidence that vascular responsiveness to adrenergic agonists is altered by both microgravity exposure (Melada *et al.*, 1975; Dickey *et al.*, 1982) and maximal exercise (Butler *et al.*, 1983; Burman *et al.*, 1985; Frey *et al.*, 1989). Peripheral vascular α-adrenergic function was decreased in primates following 14 days of horizontal casting (Dickey *et al.*, 1982) and β-adrenergic sensitivity was increased in humans following 5–14 days of bedrest (Melada *et al.*, 1975). One investigation failed to demonstrate changes in the hypertensive response to graded infusion of norepinephrine following exposure to an analogue of microgravity, suggesting no alteration in integrated adrenoreceptor responsiveness (Chobanian *et al.*, 1974). However, when selective α- (phenylephrine) and β- (isoproterenol) adrenergic agonists were infused into the subjects of the present study and blood flow was measured directly in the resting condition before and after HDT without exercise, α-adrenergic responsiveness was unchanged after HDT compared with pre-HDT, but responsiveness to β-adrenergic stimulation was increased (Convertino *et al.*, 1997). Exhaustive exercise (> 90% maximal heart rate) also increases β-adrenergic responsiveness (Butler *et al.*, 1983; Burman *et al.*, 1985; Frey *et al.*, 1989). Therefore it is possible that increased sensitivity of β-adrenergic receptors to vasodilatory agents may have contributed to restoration of peak vascular conductance following the maximal exercise treatment after HDT. However, since the percentage change in peak vascular conductance before and after HDT was poorly correlated with the percentage change in β-adrenergic responsiveness in our subjects ($r = 0{\cdot}40$) and the duration of β-adrenergic receptor upregulation after exhaustive exercise may last only 15–60 min (Frey *et al.*, 1989), it is unlikely that enhanced peak vascular conductance 24 h after exhaustive supine cycle ergometry in the present study can be explained by altered vascular responsiveness to adrenergic agonists.

In addition to the potential effect of circulating volume, vasodilator metabolites and adrenergic responsiveness on peak vascular conductance, it is possible that changes in vascular anatomy influenced peak vasodilatory responses. Since muscle capillarity is enhanced following a period of exercise training (Anderson & Hendriksson, 1977) it may be argued that the opposite would occur after a period of detraining. This notion is supported by an investigation that demonstrated a 37% reduction in capillary-to-fibre ratio of the soleus muscle in humans following 30 days' exposure to HDT (Hikida *et al.*, 1989). However, because increasing the number of capillaries has a greater effect on oxygen extraction than on tissue perfusion (Saltin, 1985), the primary contributor to blood flow is the control of peripheral vascular resistance by resistance arterioles, which dictate the redistribution of blood to exercising muscle (Mellander & Johansson, 1968). Thus, the findings of the present study raise the possibility that a single bout of maximal supine cycle ergometry may increase either the number and/or diameter of skeletal muscle resistance arterioles. This possibility is speculative, however, and awaits further investigation.

It is generally agreed that the functional limit of the cardiovascular system is defined by the peak oxygen

uptake (Rowell, 1986) which in turn is limited by oxygen transport to active muscle (Saltin & Rowell, 1980). A significant linear relationship exists between maximal oxygen uptake and maximal calf conductance (Snell *et al.*, 1987; Levine *et al.*, 1991; Martin *et al.*, 1991; Reading *et al.*, 1993; Kosmas *et al.*, 1996). This observation suggests that augmentation of leg blood flow increases oxygen delivery to the active tissue and prolongs performance time. Our data are consistent with this relationship since we observed that subjects with the highest peak vascular conductance exhibited the highest aerobic capacity before and after exposure to simulated microgravity (Fig. 5). Additionally, restoration of peak vascular conductance following performance of a single bout of supine cycle ergometry maintained time to fatigue during ischaemic plantar flexion exercise. It should be noted that peak oxygen uptake was reduced during HDT and was not completely restored following 24 h after maximal exercise. Although the relationship between peak vascular conductance and peak oxygen uptake suggests that maximal blood flow to the exercising muscle contributes to the maximal capacity to utilize oxygen, it is clearly not the only factor in determining peak oxygen uptake. This notion is consistent with previous observations that mechanisms associated with utilization of oxygen in muscle may contribute to reductions in peak oxygen uptake when mechanisms related to central cardiac effects are restored (Hikida *et al.*, 1989; Convertino, 1995).

There were limitations with this study. Since measurement of blood flow in the present investigation was initiated within 10 s after the completion of exercise and continued over 4 min, maximal blood flow could have been underestimated due to time delay with the measurement. This seems unlikely since we obtained our peak blood flows within 70 s of the end of exercise, before the time that the peak blood flow response begins to decay (Rueckert & Hanson, 1995; Fig. 3). Our measurement techniques for determination of an acute, peak increase in calf vascular conductance induced by ischaemic plantar flexion exercise represented a flow from both muscle and skin. Since a high local temperature (42°C) in combination with prolonged (10 min) ischaemia was necessary to maximally vasodilate skin in the forearm (Johnson *et al.*, 1986), it is unlikely that our ischaemic exercise protocol induced a maximal blood flow response for the entire limb, but represented primarily calf muscle blood flow. In addition, we have no data to demonstrate that 2 min of ischaemic plantar flexion exercise used in the present experiment activated all the muscles of the calf and therefore we cannot assume that all muscles were activated or that active muscles were maximally vasodilated. The notion that we did not induce maximal blood flow in the calf with ischaemic plantar flexion exercise is supported by average peak blood flows of ≈ 30 ml 100 ml^{-1} min^{-1} in the present study compared with ≈ 50 ml 100 ml^{-1} min^{-1} reported by other investigators (Johnson *et al.*, 1986; Rueckert & Hanson, 1995). Because of these limitations, we chose to use the term 'peak' rather than 'maximal' to describe the greatest increase in vascular conductance induced by ischaemic exercise under the experimental conditions of the present investigation. Since our blood flow technique was used with the application of controlled ischaemic exercise stimuli in a repeated, cross-over experimental design in which each subject served as his own control, any limitations to induce an actual maximal blood flow response did not alter our interpretation that peak vascular conductance as measured in the present experiment was reduced by exposure to low gravity and restored by performance of maximal exercise.

In summary, we observed that 16 days of continuous HDT reduced peak leg blood flow and vascular conductance to ischaemic calf exercise, but these responses were restored to pre-HDT levels when a single bout of fatiguing cycle ergometry was performed 24 h prior to the end of HDT. Peak vascular conductance was correlated with peak aerobic capacity, and restoration of the group's average peak vascular conductance with performance of maximal exercise after HDT was associated with maintenance of average time to fatigue during exhaustive ischaemic calf plantar flexion exercise.

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